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TUCKER, ELLIS & WEST LLP
1150 HUNTINGTON BUILDING
925 EUCLID AVENUE
CLEVELAND, OH 44115-1475

EXAMINER	
BARTON, JEFFREY THOMAS	
ART UNIT	**PAPER NUMBER**
1753	

DATE MAILED: 05/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/029,014	NAIR ET AL.	
	Examiner	Art Unit	
	Jeffrey T Barton	1753	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-31 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-31 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 18 September 2002 is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 12/21/01.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Drawings

1. The drawings are objected to because:

Figure 2:	The arrow to second manifold 225 is reversed. Lead lines for membranes 295 and 290 cross each other. Electrical connectors 270 and 280 are not clearly illustrated.
Figure 4:	Second interstitial volume 418 appears to be connected to inlet 440 (which is described as leading to first interstitial volume) and to the outer electrolyte zone 414. The top and bottom sections illustrated in Figure 4A are not labeled or described. The figure is unclear.

A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Specification

2. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The

disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

Several phrases using "means" are included in the abstract, in lines 9-11.

3. The disclosure is objected to because of the following informalities:

The description of the embodiment of the apparatus illustrated in Figure 4 is unclear. It is stated that "Each hollow fiber membrane 415a is positioned around a central electrode . . .", but it is not clear whether there is to be an electrode in the center of each fiber or a single central electrode (as in the other embodiments) with the fibers arrayed between this and the outer electrode.

Furthermore, in this section, reference continues to be made to the outer electrolyte zone and first and second interstitial volumes, and means for communicating sample or electrolyte to these. The first interstitial volume is clearly defined for this embodiment, but there is no reference made in the drawing or specification to membranes that would define distinct electrolyte zones or interstitial volumes (i.e. the second interstitial volume) of the type defined in the embodiments of Figure 1 A and B. In Figure 4, there appears to be no barrier between the inner and outer electrodes.

Appropriate correction is required.

Claim Objections

4. Claims 4, 13, and 22 are objected to because of the following informalities: the claim dependency is improperly stated. The phrasing, "according to any one of claims X" is not acceptable. Please revise to an appropriate form, such as, "according to claim X", "according to claims X, Y, or Z", or "according to any one of claims X, Y, or Z." In

this action, these claims were treated as being multiply dependent on claims 1-3, 10-12, and 20 and 21, respectively. Appropriate correction is required.

5. Claims 9 and 18 are objected to because of the following informalities: the claim refers to "non-planar" shapes, and lists shapes that are planar by definition. Oval and circular shapes are planar, and if rendered non-planar, would result in conical or cylindrical shapes, which are also included in the listing. Appropriate correction is required.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-4, 8-13, 17, 18, 26-29 are rejected under 35 U.S.C. 102(b) as being anticipated by Caro et al.

For claims 1 and 10, Caro et al disclose an apparatus of similar design and function, including: an inner cylindrical electrode (rod 50, Figure 5); outer concentric cylindrical electrode (pipe 52, Figure 5); first, second, and third cylindrical membranes positioned between the electrodes (36, 38, 40; Figure 5). Figure 5 illustrates the electrodes as being concentric (See also column 9 lines 8-11), which would inherently lead to a radial electric field upon application of an electric potential. Means are adapted for communication of fluids to the chambers defined by rod 50, membrane assemblies 36, 38, 40, and pipe 52. These chambers correspond to the electrolyte

zones and interstitial volumes referred to in claims 1 and 10. The means for fluid communication consist of head units 16 and 26, which include pipe stubs 37, 39, 41, and 43 with nipples 18, 20, 22, 24, 28, 30, 32, and 34 (Column 8, lines 29-50). Samples are disclosed to be introduced to chamber 62 for treatment (Column 9, lines 17-18), which corresponds to a claimed interstitial volume. Upon application of an electric field, at least one component of the sample migrates through at least one membrane (Column 9, lines 32-40).

For claims 2 and 11, Caro et al disclose the connection of rod 50 and pipe 52 as cathode and anode, respectively (Column 9, lines 32-34). Such connection would inherently involve the electrodes receiving a selected voltage, resulting in an electric potential across the intervening space.

For claims 3 and 12, Caro et al disclose an elongated housing (Column 8, lines 54-57), also illustrated in Figure 5 and evidenced by reference to membrane assembly 36 as being "3-6 feet or more in length" (Column 8, line 38) in some preferred embodiments. In addition, the head units 16 and 26, described above, are manifolds for the communication of fluids to the respective internal volumes, and are positioned at the opposing ends of the housing.

For claims 4 and 13, Caro et al disclose the use of membranes with defined pore sizes (i.e. molecular weight cutoff) in their invention (Column 4, lines 32-38).

For claims 8 and 17, Caro et al disclose the use of membranes in addition to the three generally discussed, describing an " . . . apparatus having a group of four or more chambers . . . ." See column 4, lines 39-49.

For claims 9 and 18, Caro et al claim the use of cylindrical membranes in their invention (Column 10, lines 33-34)

For claims 26 and 28, Caro et al disclose methods for using their invention as described above in the treatment of samples in the interstitial volumes (as defined in this application), including the introduction of a sample to an interstitial volume, the introduction of fluids to the electrolyte zones, the application of an electric field between the electrodes leading to the motion of at least one component of the sample across a membrane. See Column 9, lines 17-41.

For claims 27 and 29, the method discussed above further includes ". . . the purified product to be flowed out through nipple 20." (Column 9 lines 40-41), thus providing for the collection of a treated sample. In this particular listed example, Caro et al refer to the species that migrated through the membrane as the desired purified sample, but they also allow for collection of the sample from the original interstitial volume by saying that the contents of the original interstitial volume are "destined *in this case* for disposal". (italics added)

8. Claims 19 and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Stimpson.

For claim 19, Stimpson discloses an isoelectric separation device, one embodiment of which (see Figure 6) includes concentric inner and outer electrodes positioned in inner and outer buffer chambers, separated by a porous tube; and a tubular membrane disposed radially outward of the axis of the inner electrode. This is described in Column 8, lines 8-13. The electrodes are pictured in a configuration that

would lead to a radial electric field upon application of a potential across the electrodes. Additionally, the inner surface of the tubular membrane defines an interstitial volume as in the applicants' claim. Also disclosed generally for all embodiments are means adapted to communicate sample to the tubular membrane (Column 3, lines 13-16) and buffer to the buffer chambers (Column 3, lines 6-10).

This embodiment of Stimpson's invention is apparently dissimilar to the applicant's claimed invention, as illustrated with linear tubular membranes in Figure 4 of the application (though claiming a minimum of one membrane here). However, the tubular membrane in Stimpson's invention follows a radius between the inner and outer concentric electrodes, and is thus is disposed radially outward of the inner electrode axis.

For claim 30, Stimpson also discloses a method of using this apparatus by communicating buffer to the inner and outer chambers (Column 3, lines 6-10), a sample to the tubular membrane (Column 3, lines 13-16), and application of an electric field between the electrodes (Column 3, lines 27-30), which causes at least one sample constituent to move through the tubular membrane (Column 4, lines 30-42).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 5 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Caro et al in view of Margolis. Additional support is found in Bourat, Girsh et al, Broekaert et al, Dupont et al, Bredehorst et al, Kirkpatrick et al, and Benowitz et al.

Caro et al disclose a membrane separation apparatus as described above.

Caro et al do not expressly disclose the use of polyacrylamide membranes for this purpose, nor do they specify a cutoff of 1 kDa.

Margolis discloses the preparation and use of polyacrylamide membranes with varying molecular weight cutoffs for the extraction of electrophoretic fractions (Column 3, lines 51-59). Margolis further teaches the selection of a polyacrylamide gel that will give the desired pore size to the membrane that it is used to form (Column 2, lines 16-21; Column 3, lines 52-54).

Caro et al and Margolis are analogous art in that both deal explicitly with the electrophoretic separation of macromolecules using membranes.

At the time of the invention it would have been obvious to a person of ordinary skill in the art to modify the device of Caro et al by replacing one or more of the membranes with polyacrylamide membranes, as taught by Margolis, because Caro et al do not require any particular membrane material, requiring only that it be thin, flexible, and semipermeable (Column 10, lines 23-24). The polyacrylamide membranes of Margolis fulfill these requirements. In addition, it would be obvious to provide a molecular mass cutoff of 1 kDa, as selection of a proper polyacrylamide gel and degree of cross-linking would allow one to choose any cutoff needed for the desired separation. A molecular weight cutoff of 1 kDa is commonly used in the field, and was used

specifically in Bourat, Girsh et al, Broekaert et al, Dupont et al, Bredehorst et al, Kirkpatrick et al, and Benowitz et al. The fact that polyacrylamide membranes were known to have all attributes desired for a membrane in the invention of Caro et al provides the needed motivation to use them in their apparatus for any separations in which they would be advantageous.

11. Claims 6 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Caro et al in view of either Martin et al or Adachi et al.

Caro et al disclose a membrane separation apparatus as described above.

Caro et al do not expressly disclose the use of isoelectric or amphoteric membranes.

Martin et al disclose the use of isoelectric membranes in an electrophoretic separation method (Column 5, lines 50-53).

Adachi et al disclose the use of amphoteric membranes in the electrodialytic production of acids and alkalis (Column 5, lines 55-56).

Caro et al, Martin et al, and Adachi et al are analogous art in that all deal explicitly with electrophoretic separation using membranes.

At the time of the invention, it would have been obvious to a person of ordinary skill in the art to modify the device of Caro et al by replacing one or more of the membranes with isoelectric membranes, as taught by Martin et al, or amphoteric membranes, as taught by Adachi et al, because Caro et al do not require any particular membrane material, requiring only that it be thin, flexible, and semipermeable (Column 10, lines 23-24). The isoelectric membranes of Martin et al and the amphoteric

membranes of Adachi et al fulfill these requirements. Any separation requiring the use of such membranes in combination with the attributes of the apparatus of Caro et al would provide the needed motivation to use them in such an application.

12. Claims 7 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Caro et al in view of Bourat.

Caro et al disclose a membrane separation apparatus as described above.

Caro et al do not expressly disclose the use of cellulose triacetate or polyvinyl alcohol membranes.

Bourat discloses the use of cellulose triacetate membranes in an electrophoretic method (Column 8, lines 5-6).

Caro et al and Bourat et al are analogous art in that both deal explicitly with electrophoretic separation using membranes.

At the time of the invention it would have been obvious to a person of ordinary skill in the art to modify the device of Caro et al by replacing one or more of the membranes with cellulose triacetate membranes, as taught by Bourat, because Caro et al do not require any particular membrane material, requiring only that it be thin, flexible, and semipermeable (Column 10, lines 23-24). The cellulose triacetate membranes of Bourat fulfill these requirements. As cellulose triacetate membranes were known in the field, and had attributes suitable for use in a device such as that of Caro et al, one would have been motivated to use them in such a device as need dictated.

13. Claims 20, and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stimpson.

For claim 20, Stimpson discloses a device for continuous isoelectric separation, the relevant concentric embodiment of which is described in paragraph 8 above. Another relevant embodiment of this invention is illustrated in figure 4 of the patent, which discloses an array of tubular membranes disposed along a plane between two planar electrodes. This embodiment is disclosed as advantageous for apparatuses ". . . employed as a primary means of protein product recovery." (Column 7, lines 65-69).

For claim 31, methods are disclosed for the use of these embodiments, substantially as described in paragraph 8.

Stimpson does not explicitly disclose a method or apparatus using multiple tubular membranes disposed radially outward of the central electrode.

For claim 20, at the time of the invention, it would have been obvious to modify the invention of Stimpson as disclosed in Figure 6 to incorporate multiple membranes as he disclosed in Figure 4. In addition to the advantages to the apparatus shown in Figure 4 disclosed by Stimpson, when considering throughput and efficiency, the advantage of using multiple tubular membranes in a device of this type is apparent. The embodiment of figure 6 is disclosed as having the advantage of allowing compact construction. As there is no inherent impediment to using multiple membranes in the embodiment of Figure 6, one would be motivated to employ a plurality of such membranes in cases requiring the advantages of both embodiments.

For claim 31, the method of using such a modified device would have been substantially the same as that for the explicitly disclosed embodiments, and as such, would have been obvious to a person of ordinary skill in the art.

14. Claims 21 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stimpson in view of Caro et al.

For claim 21, Stimpson discloses a device for continuous isoelectric separation as described above. In addition, the device is illustrated as having an elongated housing in Figure 1.

For claim 22, Stimpson discloses the use of membranes with defined pore sizes (Column 4, lines 30-42).

Stimpson does not expressly disclose the use of manifolds as the means of communicating fluids into and out of the buffer chambers and tubular membranes.

Caro et al disclose the use of manifolds for the communication of fluids to the various chambers of their invention (Figure 5).

Caro et al and Stimpson are analogous art in that both deal explicitly with electrophoretic separation using membranes.

For claim 21, It would have been obvious to a person of ordinary skill in the art to modify the device of Stimpson by adding manifolds for the regulation of fluid flow, as taught by Caro et al. Stimpson does not discuss the specific means of ingress and egress of the various fluids needed. However, as the design of his apparatus is amenable to the use of a manifold as disclosed by Caro (having an elongated housing with two opposing ends, though which several distinct fluids are required to flow – See Figure 1), and manifolds are known to be convenient means of regulating the flow of several fluids in close proximity, one would have been motivated to use manifolds to provide for the fluid flow required in Stimpson's invention.

For claim 22, it would further have been obvious to a person of ordinary skill in the art to use membranes having defined pore sizes in such a modified invention, as they were disclosed in the original specification.

15. Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stimpson and Caro et al as applied to claim 22 above, and further in view of Margolis. Additional support is found in Bourat, Girsh et al, Broekaert et al, Dupont et al, Bredehorst et al, Kirkpatrick et al, and Benowitz et al.

Stimpson and Caro et al disclose devices for electrophoretic separation as described above.

Neither Stimpson nor Caro et al expressly disclose the use of polyacrylamide membranes with a molecular weight cutoff of at least about 1 kDa.

Margolis discloses the preparation and use of polyacrylamide membranes with varying molecular weight cutoffs for the extraction of electrophoretic fractions (Column 3, lines 51-59). Margolis further teaches the selection of a polyacrylamide gel that will give the desired pore size to the membrane that it is used to form (Column 2, lines 16-21; Column 3, lines 52-54).

Stimpson, Caro et al, and Margolis are analogous art in that all deal explicitly with the electrophoretic separation of macromolecules using membranes.

At the time of the invention it would have been obvious to a person of ordinary skill in the art to modify the combination of Stimpson and Caro et al by replacing one or more of the membranes with polyacrylamide membranes, as taught by Margolis, because neither Stimpson nor Caro et al require any particular membrane material,

requiring only that it be thin, flexible, and semipermeable (Caro - Column 10, lines 23-24) or nonionic and non-electrically conductive (Stimpson - Column 3, lines 11-12). The polyacrylamide membranes of Margolis fulfill these requirements. In addition, it would be obvious to provide a molecular mass cutoff of 1 kDa, for the reasons described in paragraph 10 and supported by the above-listed additional references. The fact that polyacrylamide membranes were known to have all attributes desired for a membrane in this device provides the needed motivation to use them for any separations in which they would be advantageous.

16. Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stimpson and Caro et al as applied to claim 22 above, and further in view of Martin et al.

Stimpson and Caro et al disclose devices for electrophoretic separation as described above.

Neither Stimpson nor Caro et al expressly disclose the use of isoelectric or amphoteric membranes.

Martin et al disclose the use of isoelectric membranes in an electrophoretic separation method (Column 5, lines 50-53).

Stimpson, Caro et al, and Martin et al are analogous art in that all deal explicitly with the electrophoretic separation of macromolecules using membranes.

At the time of the invention it would have been obvious to a person of ordinary skill in the art to modify the combination of Stimpson and Caro et al by replacing one or more of the membranes with isoelectric membranes, as taught by Martin et al, because

neither Stimpson nor Caro et al require any particular membrane material, requiring only that it be thin, flexible, and semipermeable (Caro - Column 10, lines 23-24) or nonionic and non-electrically conductive (Stimpson - Column 3, lines 11-12). The isoelectric membranes of Martin et al fulfill these requirements. As isoelectric membranes were known in the field, and had attributes suitable for use in a device such as the combination of Stimpson and Caro et al, one would have been motivated to use them in such a device for any separation that called for such a membrane.

17. Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stimpson and Caro et al as applied to claim 22 above, and further in view of Bourat.

Stimpson and Caro et al disclose devices for electrophoretic separation as described above.

Neither Stimpson nor Caro et al expressly disclose the use of membranes made of cellulose triacetate or polyvinyl alcohol.

Bourat discloses the use of cellulose triacetate membranes in an electrophoretic method (Column 8, lines 5-6).

At the time of the invention it would have been obvious to a person of ordinary skill in the art to modify the combination of Stimpson and Caro et al by replacing one or more of the membranes with cellulose triacetate membranes, as taught by Bourat, because neither Stimpson nor Caro et al require any particular membrane material, requiring only that it be thin, flexible, and semipermeable (Caro - Column 10, lines 23-24) or nonionic and non-electrically conductive (Stimpson - Column 3, lines 11-12). The cellulose triacetate membranes of Bourat fulfill these requirements. As cellulose

triacetate membranes were known in the field, and had attributes suitable for use in a device such as the combination of Stimpson and Caro et al, one would have been motivated to use them in such a device as need dictated.

Conclusion

18. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Wiechers and Lovegrove disclose three-chamber apparatuses of similar design and function.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Barton, whose telephone number is (571) 272-1307. The examiner can normally be reached Monday-Friday from 8:30 am – 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen, can be reached at (571) 272-1342. The fax number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

JTB
May 3, 2004

NAM NGUYEN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1700